IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Van Quaquebeke, et al.
Appl. No.	:	10/530,904
Filed	:	December 23, 2005
For	:	2" OXO-VORUSCHARIN AND DERIVATIVES THEREOF
Examiner	:	Badio, Barbara
Group Art Unit	:	1617

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

1. I am an inventor in the above-identified application.

2. I am familiar with the specification of US Application No. 10/530,904 and with the Office Action of November 15, 2006. This Declaration presents *in vitro* and *in vivo* data to show that compounds as described in the specification are effective in treating prostate and pancreatic cancer.

3. The efficacy of Compound B on the growth of two different human cancer cell lines was tested *in vitro* using the MTT test as described in Example 3 of the present specification. The cell lines tested were PC-3 (Prostate) and Capan-2 (Pancreas). The IC_{50} value of Compound B on PC-3 cell line ranged from 10^{-8} M to 5×10^{-9} M. The IC_{50} value of Compound B on Capan-2 cell line was 10^{-9} M. Based upon these results, I conclude that Compound B has anti-tumor activity for both the PC-3 and Capan-2 cell lines, corresponding to marked decreases in the overall growth of prostate and pancreatic human cancer models.

4. Compound B was evaluated *in vivo* on highly invasive orthotopic PC-3 refractory prostate cancer model by measurement of T/C index, as described in Example 6 of the specification. Both *i.p.* and *per os* administration of Compound B (*i.p.* at DMT/4 (20 mg/kg), 5 injections per week on Monday, Tuesday, Wednesday, Thursday, and Friday, during 6 consecutive weeks

(5ix6w) and *per os* at DMT/2 (40 mg/kg) 5 doses per week on Monday, Tuesday, Wednesday, Thursday, and Friday, during 6 consecutive weeks (5dx6w)) very significantly increased the survival periods of PC-3 orthotopic xenograft-bearing nude mice. T/C values of 177% with *i.p.* administration and 132 % with *per os* administration were obtained (Figure 1). In both cases, the mice were treated from the 7th day post-graft. I conclude that Compound B exerts a significant anti-tumor effect on the highly invasive orthotopic PC-3 refractory prostate cancer model.

5. Compound B was evaluated on *in vivo* orthotopic Capan-2 pancreatic cancer model by measurement of T/C index, as described in Example 6 of the specification. In a first set of experiments, *i.p.* administration of Compound B at DMT/4 (20 mg/kg), 3 injections per week on Monday, Wednesday, and Friday, during 5 consecutive weeks (3ix5w) increased the survival periods of Capan-2 orthotopic xenograft-bearing nude mice, with T/C value of 129% (Figure 2a). In a second set of experiments, *i.p.* administrations of Compound B at DMT/8 (10 mg/kb – 5 injections per week on Monday, Tuesday, Wednesday, Thursday, and Friday, during 8 consecutive weeks (5ix8w) increased the survival periods of Capan-2 orthotopic xenograft-bearing nude mice, with a T/C value of 127% (Figure 2b). For the first set of experiments, the mice were treated from the 21st day post-graft. For the second set of experiments, the mice were treated from the 14th day post-graft. I conclude that Compound B exerts a significant anti-tumor effect on the orthotopic Capan-2 pancreatic cancer model.

6. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States codes and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: 13.02.2007 By: FRANCIS DARRO

3417105
021207